Attorney Docket No.: 6056-236 (35926-136495)
AMENDMENT AND REPLY UNDER 37 C.F.R. § 1.111

SUBMISSION OF FORMAL DRAWINGS

In response to the Notice of Draftsperson's Patent Drawing Review, one set of formal drawings, consisting of eleven (11) sheets was filed on June 30, 2003.

REMARKS

Claims 1-33 were pending. Claims 13-19, 23 and 33 have been withdrawn from consideration as they are directed to non-elected species. Claims 1-12, and 20-21 have been amended. Upon entry of the present amendments, Claims 1-33 will be pending in this application and Claims 1-12, 20-22, and 24-32 are under active examination.

The claims have been amended to more particularly and distinctly claim that which Applicants regard as their invention. In particular, Claims 1-3 have been amended to provide the full names of *E. carinatus*, HPLC and VCAM-1 as requested by the Examiner. Claims 4-11, and 21, have been amended to correct the antecedent basis of these claims. Claim 20 is amended to delete the language "biologically active fragment or derivative thereof".

The specification has been amended to correct certain informalities therein. In particular, the specification has been amended to capitalize the Trademark name "LICHROSHPER", and to provide the full name and capitalize "TRITON X". The specification has also been amended to delete "X" from the RGD motif on page 38. Support for this amendment can be found in the specification, *inter alia*, on pages 2, 3, 6, 8, and 13.

The amendments to the claims and the specification do not constitute new matter as defined under 35 U.S.C. § 132. Applicants respectfully request entry of the amendments.

I OBJECTIONS TO THE SPECIFICATION AND CLAIMS

The Examiner objects to certain informalities in the specification and claims. In particular, the Examiner objects to the specification for disclosing RGDX without having its corresponding SEQ ID NO.

Applicants have amended the specification to delete the letter "X" from RGDX. Applicants submit that the letter "X" is not directed to any specific amino acid sequence and its presence solely suggests that RGD can be attached to other amino acid sequence or other moieties. As is evident from the specification, RGD is the recognition site for many disintegrins and as such it can be a part of different peptides. See, the specification, *inter alia*, at pages 2, 3 and 13 and (GRGDSP- SEQ ID NO:12), (RGDS- SEQ ID NO: 15), and (KRARGDDMDDY- SEQ ID NO: 4). Accordingly, deletion of "X" from RGD does not materially change RGD and does not add new matter as defined under 35 U.S.C. § 132. Applicants further submit that "RGD" as amended contains less than four amino acids and therefore, pursuant to 37 C. F. R. § 1.821 (a), no SEQ ID NO. is required to identify this molecule.

The Examiner objects to the use of the names Lichospher and Triton X in pages 31 and 33 of the specification, respectively. The Examiner requires these names to be capitalized in the specification and their generic names to be provided. Applicants have amended the specification to capitalize the names "Lichospher" and "Triton X". The generic name of TRITON X is also provided. Additionally, as disclosed in the specification, at page 31, LICHOSPHER is a brand name of a HPLC column therefore, no generic name is required.

The Examiner objects to Claim 20 as having a typographical error in the word "echistatin". Applicants have amended Claim 20 to correct the typographical error noted by the Examiner.

II. REJECTION OF CLAIMS UNDER 35 U. S. C. § 112, SECOND PARAGRAPH

The Examiner rejects Claims 1-3, 4, 6, 8-12, 20-22 and 24-32 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as their invention.

Specifically, the Examiner states that Claims 1-3, 24-30 and 32, recite abbreviations and are thus deemed indefinite. Applicants have amended Claims 1-3, 24-30 and 32 to provide the full names of the abbreviations cited therein. Accordingly, the Examiner's rejection of these claims is rendered moot.

The Examiner rejects Claims 4, 6-10 and 20 for the recitation of the phrase "biologically active fragments". Specifically, the Examiner states that:

> "[T]he phrase is so broad as to be essentially useless. Even a fragment of an amino acid has some biological activity. What is encompassed by a biological activity of EC-3 is not defined."
>
> Office Action, page 3, Paper No 18

Applicants respectfully submit that the metes and bounds of the claims with respect to the "biologically active fragments" in view of the specification are abundantly clear. The specification describes that a biologically active fragment is a fragment of an EC-3 peptide which retains at least one biological activity of the EC-3 peptide. The biological activity of the EC-3 protein and peptide fragments thereof are amply described in the specification and the original claims as filed.

The Examiner believes the term "biologically active fragment" is vague because any fragment of a peptide has some biological activity. Applicants respectfully submit that, as is evident from the language of the claims, biologically active fragments of the peptides of the invention as claimed must possess all limitations of peptides of the base claim from which they derive. For example, a biologically active fragment of an EC-3 peptide, as claimed in Claim 4, must possess the ability to inhibit adhesion of Jurkat cells to vascular cell adhesion molecule-1, as claimed in Claim 1, and other characteristics of the EC-3 peptide as claimed in Claim 2. Therefore, contrary to the Examiner's contention, biologically active fragments of an EC-3

peptide are more than adequately defined to meet the requirement of Section 112, second paragraph.

The Examiner rejects Claim 20 for reciting an amino acid sequence without reciting the representative SEQ ID NO. Applicants' amendment to Claim 20 that recites the requisite SEQ ID NO. 9 overcome the Examiner's rejection of this claim.

The Examiner rejects Claim 21 for the recitation of "a peptide that binds the integrin of interest from venom." Applicant's amendment to Claim 21 that clarifies the language of this claim with respect to the integrin and venom overcome the Examiner's rejection of this claim.

The Examiner rejects Claims 31 and 32, as the Examiner believes it is unclear what is meant by "substantial homology." Specifically, the Examiner states: "[H]ow similar must the primary structure of a peptide be to have "substantial homology with SEQ ID NO:2?" Applicants respectfully submits that the language "substantial homology" of Claims 31 and 32 satisfies 35 U. S. C. § 112, second paragraph's requirement in that the skilled artisan, upon reading claims in view of the specification, would readily appreciate the metes and bounds of the "substantial homology with SEQ ID NO:2" of the invention. The Examiner's attention is respectfully directed to the specification, *inter alia,* on page 14, which describes that "substantial amino acid sequence homology" means an amino acid sequence homology greater than about 30 percent, preferably greater than about 60%, more preferably greater than about 80%, and most preferably greater than about 90 percent.

In view of the above, Applicants respectfully request reconsideration and withdrawal of this rejection.

III. REJECTION OF CLAIMS UNDER 35 U. S. C. § 102 (a)

The Examiner rejects Claims 4, 6, 8, 20, 22 and 24-27 under 35 U.S.C. §102(a) as being allegedly anticipated by Vanderslice *et al.* Specifically, the Examiner states that:

> "[V]andersclice *et al.* provides peptides that are antagonists of α_4 integrins. The assays included inhibition $\alpha_4\beta_1$ and $\alpha_4\beta_7$ binding to receptors expressed on cell surfaces, such as V-CAM, CS-1 and Mad-CAM. This reference is deemed anticipatory for the claimed subject matter because by sufficient deletions and substitutions, the peptides of Table 1 of the reference could be considered

derivatives of EC3 peptides which retain the biological activity of binding α_4 integrins.

Office Action, page 4, Paper No. 18.

Applicants respectfully traverse the Examiner's rejection.

As a preliminary matter, Applicants believe that the Examiner's basis for an anticipation rejection is untenable. As the Examiner is no doubt aware, the standard governing anticipation under 35 U. S. C. §102 is one of strict identity. Anticipation can only be established by a prior art reference which discloses each and every element of the claimed invention; anticipation is not shown even if the differences between the claims and the prior art references are argued to be "insubstantial" and that the assertion of invalidity for lack of novelty is erroneous if the prior art disclosed "substantially the same thing". The prior art references in question must meet each claim limitation in order to constitute anticipation. *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 225 U.S.P.Q. 253 (Fed. Cir. 1985). The prior art reference must disclose, either expressly or under the principles of inherency, every limitation of the claim in issue. *Corning Glass Works v. Sumitomo Elec. U.S.A., Inc.*, 868 F.2d 1251, 1255- 56 (Fed. Cir. 1989).

Applicants respectfully submit that Vanderslice *et al*, does not teach or suggest, either expressly or inherently, the claimed invention. Vanderslice *et al.*'s antagonists of α_4 integrins are cyclic hexapeptides having the amino acid sequence of CWLDVC. The cyclic hexapeptides of Vanderslice *et al.* were synthesized by a peptide synthesizer based on the LDV sequence of CS1. (Vanderslice *et al.*, Abstract and material and methods "peptide synthesis", page 1711). The peptides of the invention as claimed are directed to a substantially purified EC-3 protein, or subunits thereof, isolated from *Echis carinatus* venom, characterized by: (a) an apparent molecular mass of about 14,762 Da, as determined by electrospray ionization mass spectrometry; (b) elution from a C-18 HPLC column at about 40% acetonitrile; and (c) the ability to inhibit adhesion of Jurkat cells to VCAM-1. None of these characteristics, either expressly or inherently, are disclosed for the peptides of Vanderslice *et al.*

The Examiner contends that Vanderslice *et al.* is deemed anticipatory for the claimed peptides because by sufficient deletions and substitutions the peptides of Table 1 of Vandersclice

et al.'s peptides could be considered derivatives of EC3 peptides of the invention which retain the biological activity of binding α_4 integrins.

Applicants respectfully submit that Vanderslice *et al.* does not anticipate the biologically active fragments of EC3 peptides as claimed because, as stated above, this reference does not teach each every element of the base claim (*i.e.*, Claim 1) from which claims 4, 6, 8, and 20 are dependant from.

In view of the foregoing reasons, Vanderslice *et al.* is not anticipatory prior art against Claims 4, 6, 8, 20, 22 and 24-27 of this invention. Reconsideration and withdrawal of this rejection is respectfully requested.

IV. REJECTION OF CLAIMS UNDER 35 U. S. C. § 102 (b)

The Examiner rejects Claims 4, 6, 8, 20 and 22 under 35 U.S.C. § 102(b) as allegedly being anticipated by the compound of "glycine" described in Merck Index. Specifically, the Examiner states that:

> "[T]his rejection is based on the recitation of a biologically active fragment. The amino acid is anticipatory for the claimed subject matter because it is a fragment of the disclosed polypeptide(s) and is known to be biologically active."

Office Action, page 5, Paper No. 18.

Applicants respectfully traverse the Examiner's rejection for the following reasons.

The Examiner's basis for this rejection is the same as discussed under Section III above. Applicant's response under Section III above, therefore, equally applies to this rejection. In short, the Examiner believes that a peptide of one amino acid long, such as "glycine" disclosed in Merck Index, with any biological activity is encompassed within the scope of the rejected claims. Applicants respectfully submit that, for the reasons stated above, the Examiner's analysis of the language of "biologically active fragment and/or derivatives of EC3 peptides" is in vacuum and out of context and therefore legally untenable.

Reconsideration and withdrawal of this rejection is respectfully requested.

V. REJECTION OF CLAIMS UNDER 35 U. S. C. § 103

The Examiner rejects Claims 28-30 under 35 U.S.C. § 103(a) as being unpatentable over Vanderslice *et al.* Specifically, while the Examiner notes that Vanderslice *et al.* does not teach the administration of the peptides to animals, it is the Examiner's position that such would be obvious to one of ordinary skill in the art.

Applicants respectfully traverse the Examiner's rejections.

As stated under Sections III and IV above, Vanderslice *et al.*, does not teach or suggest the substantially purified EC-3 protein and peptide fragments thereof isolated from *E. Carinatus* venom as required by the claimed invention. Accordingly, contrary to the Examiner's assertion, administration of the cyclic peptides of Vanderslice *et al.* to animals does not render the method of the invention as claimed in Claims 28-30 obvious. Accordingly, Vanderslice *et al.* is not a proper reference under Section 103 against any claims of this application.

CONCLUSION

In light of the above, Applicants respectfully submit that all pending claims are allowable over the art of record, and a Notice of Allowance is courteously solicited. The foregoing is submitted as a full and complete response to the Office Action mailed April 10, 2003 (Paper No. 18). The Examiner is invited and encouraged to contact the undersigned attorney of record if such contact will facilitate an efficient examination and allowance of the application.

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Respectfully submitted,

STEFAN NIEWIAROWSKI *et al.*

By: _____

DANIEL A. MONACO
Registration No. 30,480
Drinker, Biddle Reath, LLP
One Logan Square
18th and Cherry Streets
Philadelphia, PA 19103-6996
(215) 988-3312
Attorney for Applicants